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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/693,712	10/27/2003	Hideki Taniguchi	25682	2281
20529	7590	07/11/2007		
NATH & ASSOCIATES 112 South West Street Alexandria, VA 22314			EXAMINER	
			POPA, ILEANA	
			ART UNIT	PAPER NUMBER
			1633	
			MAIL DATE	DELIVERY MODE
			07/11/2007	PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

**Office Action Summary**

Application No.

10/693,712

Applicant(s)

TANIGUCHI ET AL.

Examiner

Ileana Popa

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 13 April 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 11-24, 40-55, 57-90 and 3037 is/are pending in the application.
- 4a) Of the above claim(s) See Continuation Sheet is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 11-13, 18-21, 30, 31, 40-48, 51, 52, 75, 76, 79, 80, 83, 84, 85, and 88 is/are rejected.
- 7) ☒ Claim(s) 11-13, 30, 31 and 40-48 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |                                                                                                            |                                                                                         |
|------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                                           | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____                                                |

Continuation of Disposition of Claims: Claims withdrawn from consideration are 14-17,22-24,32-37,49,50,53-74,77,78,81,82,86,87,89 and 90.

### DETAILED ACTION

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in the prior Office Action.
2. Claims 1-10, 25-29, 38, 39, and 56 have been cancelled. Claims 75-90 are new. Claims 11-13, 18, 19, 30, 31, and 40-48 have been amended. Claims 14-17, 22-24, 32-37, 49, 50, and 53-74 have been withdrawn.

Newly submitted claims 77, 78, 81, 82, 86, 87, 89, and 90 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: the new claims 77, 78, 81, 82, 86, 87, 89, and 90 introduce new limitations that require a distinct search from the search required for the originally presented invention. For example claims 77, 78, 81, 82, 86, 87, 89, and 90 are drawn to a method of identifying a pancreatic stem cell that uses different steps and compositions as compared to the method of separating pancreatic stem cells, such as isolating mRNA and probes/primers for genes encoding cell surface markers.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 77, 78, 81, 82, 86, 87, 89, and 90 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Newly submitted claims 75, 76, 79, 80, 83, 84, 85, and 88 are encompassed by the elected invention.

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Claims 11-13, 18-21, 30, 31, 40-48, 51, 52, 75, 76, 79, 80, 83, 84, 85, and 88 are under examination.

### ***Claim Objections***

3. Claims 11-13, 30, 31, and 40-48 objected to under 37 CFR 1.75(c) as being in improper form because they are directly or indirectly dependent from subsequent claims.

### ***Response to Arguments***

#### ***Priority***

4. Acknowledgment is made of Applicant's submission of an English language translation of the priority document, PCT/JP0204084. However, Applicant did not provide a statement that the translation of the certified copy is accurate in accordance with 37 C.F.R. 1.55. Therefore, the priority date for the instant application is still considered to be 10/27/2003.

#### ***Double Patenting***

5. The objection to claims 7-10 and 25-29 as being a substantial duplicates of claims 1-5 is moot because Applicant cancelled the claims in the response filed on 04/13/2007.

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6. The objection to claims 41, 42, and 45 as being a substantial duplicates of claims 40 and 43 is withdrawn in response to Applicant's amendments to the claims filed on 04/13/2007.

***Claim Rejections - 35 USC § 101***

7. The rejection of claims 11-13 and 40-48 under 35 U.S.C. 101 for being directed to non-statutory subject matter is withdrawn in response to Applicant's amendments to the claims filed on 04/13/2007.

***Claim Rejections - 35 USC § 112, 2<sup>nd</sup> paragraph***

8. The rejection of claims 28 and 29 under 35 U.S.C. 112, second paragraph, as being indefinite, is moot because Applicant cancelled the claims in the response filed on 04/13/2007.

The rejection of claims 13, 30, 31, and 47 under 35 U.S.C. 112, second paragraph, as being indefinite is withdrawn in response to Applicant's amendments to the claims filed on 04/13/2007.

9. The rejection of claims 1-10, 25-29, 38, 39, and 56 under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, is moot because Applicant cancelled the claims in the response filed on 04/13/2007.

The rejection of claims 30 and 31 under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, is withdrawn in response to Applicant's amendments to the claims filed on 04/13/2007.

***Claim Rejections - 35 USC § 112 – written description***

10. The rejection of claims 1, 2, 4, and 5 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is moot because Applicant cancelled the claims in the response filed on 04/13/2007.

***Claim Rejections - 35 USC § 112 – enablement***

11. Claims 1-10, 25-29, 38, 39, and 56 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement is moot because Applicant cancelled the claims in the response filed on 04/13/2007.

The rejection of claims 11 and 40-42 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement is withdrawn in response to Applicant's amendments to the claims filed on 04/13/2007.

***Claim Rejections - 35 USC § 103***

12. The rejection of claims 1-10, 18-21, 25-29, 38, 39, and 56 under 35 U.S.C. 103(a) as being unpatentable over Ramyia et al. (Nature Medicine, 2000, 6: 278282), in view of Serup (Nature Genetics, 2000, 25: 134-135), Oberg-Welsh et al. (Pancreas,

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1996, 12: 334-339), and Suzuki et al. (Hepatology, 2000, 32: 1230-1239) is moot because Applicant cancelled the claims in the response filed on 04/13/2007.

13. Claims 11-13, 18-21, 30, 31, 40-48, 51, 52 remain and the new claims 75, 76, 79, 80, 83, 84, 85, and 88 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ramyia et al., in view of each Serup, Oberg-Welsh et al., and Suzuki et al. for the reasons of record set forth in the non-final Office action. Applicant's arguments filed on 04/13/2007 have been fully considered but they are not persuasive.

Applicant traversed the instant rejection on the grounds that (i) Ramyia et al. teach *in vitro* growth of islets from stem cells and detection of transcripts for insulin, insulin receptor, hepatocyte growth factor, and c-met by RT-PCR without teaching separating the pancreatic stem cells by using antibodies against c-Met, c-kit, CD45, TER119, and Flk, (ii) Serup teaches that there are no reliable surface markers for pancreatic stem cells, (iii) Oberg-Welsh et al. teaches the expression of Flk1 in insulin-producing cells, (iv) Suzuki et al. teach separation of hepatic progenitor cells by flow cytometry. Applicant argues that there is no motivation to support the combination of the cited references and that none of the cited references, alone or together, teach or suggest all the limitation of the instant claims, i.e., selecting the claimed markers and separating the stem cells by contacting them with the antibodies directed to the claimed markers. Therefore, Applicant requests the withdrawal of the rejection.

Applicant's arguments are acknowledged, however, the rejection is maintained for the following reasons:



In response to Applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

The prior art teaches that isolation of pure population of stem cells requires antibodies against several cell surface markers. With respect to the pancreatic stem cells, the art teaches the need of identifying pancreatic stem cells markers to be used in their isolation, wherein isolated pancreatic stem cells are useful for therapy (see Serup, Abstract, p. 134, column 1 bridging column 2, and column 3, p. 135, column 3). While it is true that Serup teaches that there are no reliable surface markers, the markers are suggested by the prior art. Ramyia et al. teach that pancreatic ductal stem cells express c-Met. Oberg-Welsh et al. teach that c-kit and Flk-1 are specifically expressed in the pancreatic ducts where the pancreatic stem cells reside, and not in the endocrine and exocrine pancreas, and suggest that these receptors could play a role in the differentiation of ductal precursor cells (Abstract, p. 336, column 2, p. 337, column 2, second paragraph p. 338, column 1, first paragraph). Suzuki et al. teach the using antibodies directed against CD45 and TER119 to exclude contaminating hematopoietic cells expressing these markers from stem cell preparations (p., 1231, column 1, second paragraph, p. 1232, column 1). Therefore, one of skill in the art would have known to use antibodies against c-Met, c-kit, and Flk-1 because the art teaches that these cell surface markers are expressed by pancreatic stem cells. While other surface markers

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beside c-Met, c-kit, and Flk-1 are expressed (for example insulin, IGF-1, and FGF receptors), these markers are also expressed by the endocrine and exocrine pancreas (devoid of pancreatic stem cell) and therefore, one skill in the art would not have been motivated to use these surface markers to separate pancreatic stem cells; similarly, in response to Applicant's enumeration of other genes identified by Ramyia et al. and Oberg-Welsh et al., such as growth factors and intracellular proteins (transcription factors and proteins involved in intracellular signaling), it is noted that one of skill in the art have known that they all are not cell surface markers and therefore could not be used to separate cells by flow cytometry. In addition to the above, one of skill in the art would have been motivated to use antibodies to the cell surface markers CD45 and TER119 in order to eliminate contaminating hematopoietic cells, as taught by Suzuki et al. Therefore, Applicant's argument that Suzuki et al. is not pertaining art because they teach isolation of hepatic progenitor cells is not found persuasive because it is the teaching of eliminating contaminating hematopoietic cells that would have motivated one of skill in the art to use these antibodies. Thus, the claimed invention was *prima facie* obvious at the time the invention was made.

With respect to the arguments that none of the cited references teaches or suggests contacting the pancreatic stem cells with probes or primers, as required by claims 77, 78, 81, 82, 86, 87, 89, and 90, it is noted that claims 77, 78, 81, 82, 86, 87, 89, and 90 have been withdrawn from consideration for being drawn to a non-elected invention.

***Conclusion***

14. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

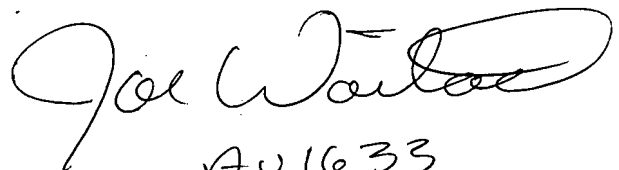
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ileana Popa whose telephone number is 571-272-5546. The examiner can normally be reached on 9:00 am-5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Ileana Popa, PhD

  
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